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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.
09/300,978	04/28/99	SPITLER	L 204372000301

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EXAMINER	
GAMBEL, P	
ART UNIT	**PAPER NUMBER**
1644	

DATE MAILED: 10/11/00

Please find below and/or attached an Office communication concerning this application or proceeding.

Commissioner of Patents and Trademarks

Office Action Summary

Application No.	Applicant(s)
09/300978	SPITLER ET AL.
Examiner	**Group Art Unit**
GAMBEL	1644

—The MAILING DATE of this communication appears on the cover sheet beneath the correspondence address—

Period f r Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, such period shall, by default, expire SIX (6) MONTHS from the mailing date of this communication .
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).

Status

☑ Responsive to communication(s) filed on 7/17/00.

☐ This action is **FINAL**.

☐ Since this application is in condition for allowance except for formal matters, **prosecution as to the merits is closed** in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 1 1; 453 O.G. 213.

Disposition of Claims

☑ Claim(s) 13-24 is/are pending in the application.

Of the above claim(s)____ is/are withdrawn from consideration.

☐ Claim(s)____ is/are allowed.

☑ Claim(s) 13-24 is/are rejected.

☐ Claim(s)____ is/are objected to.

☐ Claim(s)____ are subject to restriction or election requirement.

Application Papers

☐ See the attached Notice of Draftsperson's Patent Drawing Review, PTO-948.

☐ The proposed drawing correction, filed on____ is ☐ approved ☐ disapproved.

☐ The drawing(s) filed on____ is/are objected to by the Examiner.

☐ The specification is objected to by the Examiner.

☐ The oath or declaration is objected to by the Examiner.

Pri rity under 35 U.S.C. § 119 (a)-(d)

☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 11 9(a)-(d).

☐ All ☐ Some* ☐ None of the CERTIFIED copies of the priority documents have been

☐ received.

☐ received in Application No. (Series Code/Serial Number)____.

☐ received in this national stage application from the International Bureau (PCT Rule 1 7.2(a)).

*Certified copies not received:____.

Attachment(s)

☑ Information Disclosure Statem nt(s), PTO-1449, Paper No(s). 3

☐ Interview Summary, PTO-413

☑ Notice of Reference(s) Cited, PTO-892

☐ Notice of Informal Patent Application, PTO-152

☐ Notice of Draftsperson's Patent Drawing Review, PTO-948

☐ Other____

Office Action Summary

DETAILED ACTION

1. Upon reconsideration of applicant's arguments and in the interest of compact prosecution, claims 13-24 as it reads on methods of eliciting antitumor responses with both PSMA and PSMA encoding nucleic acids, as the elected species, are under consideration in the instant application.

Claims 1-12 have been canceled previously.

2. Applicant should amend the first line of the specification to update the status of the priority documents.

3. The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. Applicant should restrict the title to the claimed invention.

4. The Abstract of the Disclosure is objected to because it does not adequately describe the claimed invention. Correction is required. See MPEP 608.01(b).

5. The application is required to be reviewed and all spelling, TRADEMARKS, and like errors corrected.

Trademarks should be capitalized or accompanied by the ™ or ® symbol wherever they appear and be accompanied by the generic terminology. Although the use of trademarks is permissible in patent applications, the proprietary nature of the trademarks should be respected and every effort made to prevent their use in any manner which might adversely affect their validity as trademarks.

Appropriate corrections are required

6. The following is a quotation of the first paragraph of 35 U.S.C. § 112:
The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 13, 17-24 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

The instant claims are drawn to methods of eliciting antitumor responses to prostate tumors by administering:
A) "at least one antigen over represented in the prostate gland or an immunologically effective portion thereof";
B) "nucleic acid that generate said antigen or antigens in situ".

Such "over represented antigens" and "nucleic acid sequences" do not meet the written description provision of 35 USC 112, first paragraph. There is insufficient guidance and direction as to the written description of these "over represented antigens" and "nucleic acid sequences.

Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that [he or she] invented what is claimed." (See Vas-Cath at page 1116.)

The skilled artisan cannot envision the detailed chemical structure of the encompassed polynucleotides (proteins) and therefore conception is not achieved until reduction to practice has occurred, regardless of the complexity or simplicity of the method of isolation. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for isolating it. The nucleic acid itself is required. See Fiers v. Revel, 25 USPQ2d 1601, 1606 (CAFC 1993) and Amgen Inc. V. Chugai Pharmaceutical Co. Ltd., 18 USPQ2d 1016.

One cannot describe what one has not conceived. See Fiddes v. Baird, 30 USPQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class. The specification provided only the bovine sequence. Thus, the specification fails to describe these DNA sequences. The Court further elaborated that generic statements are not an adequate written description of the genus because it does not distinguish the claimed genus from others, except by function. Finally, the Court indicated that while applicants are not required to disclose every species encompassed within a genus, the description of a genus is achieved by the recitation of a representative number of DNA molecules, defined by nucleotide sequence, falling within the scope of the genus, See The Regents of the University of California v. Eli Lilly and Company, 43 USPQ2d 1398, 1406 (Fed. Cir. 1997).

It is noted that pages 7-10 of the specification as filed does not provide for over represented prostate antigens other than PSA, PSMA and PAP (see Illustrative Antigens)
Also, it is acknowledged that here the specification discloses certain references for the nucleic acids for PSA, PSMA and PAP; but that such nucleic acid sequences are not disclosed in the specification as file. See Section below

Applicant is reminded that Vas-Cath makes clear that the written description provision of 35 USC 112 is severable from its enablement provision. (See page 1115.) Applicants are directed to the Revised Interim Guidelines for the Examination of Patent Applications Under the 35 U.S.C. 112, ¶ 1 "Written Description" Requirement, Federal Register, Vol. 64, No. 244, pages 71427-71440, Tuesday December 21, 1999.

Therefore, there is insufficient written description for "at least one antigen over represented in the prostate gland or an immunologically effective portion thereof" and "nucleic acid that generate said antigen or antigens in situ". other than that disclosed in the specification as filed under the written description provision of 35 USC 112, first paragraph.

6. Claims 13-24 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for "full-length PSA, PSMA and PAP"; does not reasonably provide enablement for any "over represented prostate specific antigen" and "immunologically effective portion thereof". The specification does not enable any person skilled in the art to which it pertains, or with which it is most clearly connected, to make and use the invention commensurate in scope with these claims.

Applicant has not provided sufficient biochemical information (e.g. molecular weight, amino acid composition, N-terminal sequence, etc.) that distinctly identifies "over represented prostate antigens" other than "PSA, PAP or PSMA". While "over represented prostate antigen" and "immunologically effective portion thereof" may have some notion of the claimed active ingredients; there is insufficient direction and guidance which enables the skilled artisan to make and use "over represented prostate specific antigen" and "immunologically effective portion thereof", commensurate in scope with the claimed invention.

Appellant has not enabled the breadth of the claimed invention in view of the teachings of the specification. Factors to be considered in determining scope and enablement are: 1) quantity of experimentation necessary, 2) the amount of direction or guidance presented in the specification, 3) the presence or absence of working examples, 4) the nature of the invention, 5) the state of the prior art, 6) the relative skill of those in the art, 7) the predictability or unpredictability of the art, and 8) the breadth of the claims. See Ex parte Forman, 230 USPQ 546, BPAI, 1986.

Appellant has not disclosed how to use the claimed vaccines and methods to treat prostatic cancer as a therapeutic regimen in humans. There is insufficient evidence of the invention with respect to the in vivo operability of the claimed prostate-specific proteins, peptides or fragments thereof as well as anti-idiotypic antibodies to use appellant's invention.

Pharmaceutical therapies in the absence of in vivo clinical data are unpredictable for the following reasons; (1) the protein may be inactivated before producing an effect, i.e. such as proteolytic degradation, immunological inactivation or due to an inherently short half-life of the protein; (2) the protein may not reach the target area because, i.e. the protein may not be able to cross the mucosa or the protein may be adsorbed by fluids, cells and tissues where the protein has no effect; and (3) other functional properties, known or unknown, may make the protein unsuitable for in vivo therapeutic use, i.e. such as adverse side effects prohibitive to the use of such treatment. See page 1338, footnote 7 of Ex parte Aggarwal, 23 USPQ2d 1334 (PTO Bd. Pat App. & Inter. 1992).

In vitro and animal model studies have not correlated well with in vivo clinical trial results in patients. Concerning vaccines to elicit antitumor responses in general, the antigenic or immunogenic nature of a protein or an anti-idiotypic antibody does not necessarily correlate with its ability to confer antitumor responses.

As disclosed on page 2, paragraph 1 of the instant specification; applicant discloses that prostate cancer continues to be refractory to treatment despite many years of efforts to improve therapy. Similarly, appellant discloses that at the time the invention was made; vaccine development has been slow and no vaccine approved by the FDA for marketing currently exists for any form of cancer.

Appellant has not provided sufficient objective evidence that predicts the efficacy of the instant invention drawn to "over represented prostate antigens" or" immunologically active portions of PSA, PSMA or PAP" in the specification as filed or a portion thereof for the treatment or prevention of human prostatic cancer.

As the instant inventor acknowledges (Spitler, Cancer Biotherapy 10:1-3, 1995; page 1, column 1, paragraph 1; 1449); "Ask practicing oncologists what they think about cancer vaccines and you're likely to get the following response: "cancer vaccines don't work". Ask a venture capitalist or the director of product development at a large pharmaceutical company, and you're likely to get the same response". Therefore, applicant has recognized the lack of predictability of the nature of the art and state of the prior art to which the instant invention pertains, as similarly disclosed on page 2 of the specification. Also, such disclosures clearly indicate that the amount of direction or guidance presented in the specification is limited, and would not permit a person skilled in the art to use the invention without undue experimentation at the time the invention was made.

Furthermore, Hodge et al. (Int. J. Cancer 63: 231-237, 1995; 1449) discloses that previous attempts to actively immunize patients with prostate adenocarcinoma cells admixed with adjuvant shown little or no therapeutic benefit (page 231, column 1, first paragraph of Introduction). Here, the reference discloses that these previous attempts to actively immunize were known in 1990, prior to appellant's invention. Such prostate adenocarcinoma cells and normal prostate cells express common antigens. Therefore, targeting prostate-specific antigens that are expressed on both normal and tumor cells in cancer immunotherapy to target tissue-specific antigens was known and practiced at the time the invention was made.

With respect to prostate-specific immunotherapy, Hodge et al. (Int. J. Cancer, 1995; 1449) discloses that previous attempts to actively immunize patients with prostate adenocarcinoma cells admixed with adjuvant shown little or no therapeutic benefit (page 231, column 1, first paragraph of Introduction). Models of evaluation of prostate therapeutics including the canine and the Dunning rat are not practical for PSA-recombinant vaccines due to the very low homology of rat and canine PSA to human PSA (page 231, column 2, paragraph 2). The fact that human PSA is a secreted antigen should be taken into consideration for its potential use as a target for human prostate cancer, as the secreted antigen may also reduce immunoglobulin responses by forming antigen-antibody complexes and/or potentially anergizing specific T cell responses (page 235, column 1, lines 1-6). An immune reaction directed against PSA could lead to side effects resulting from cross-reactivity with other kallikrein family members (page 235, column 2, lines 4-6). Therefore, the use of prostate-specific antigens in vaccines are likely to be limited by either neutralization by secreted prostate antigen or by inducing autoimmunity. Although the recombinant human PSA construct was unable to elicit an anti-PSA IgG response, PSA-specific IgM response were noted in all immunized monkeys (page 236, column 1, paragraph 1). However, these antibody responses were of low titer, were short-lived and could not be boosted. It is noted that the monkeys developed in vitro lymphoproliferative responses to PSA (page 236, column 1, paragraph 2). However, it is not clear that such studies can be extrapolated to humans because in the difference in MHC motifs between rhesus and humans and the levels of expression of class I and II MHC on rhesus vs. human prostate and human normal prostate vs. prostate carcinoma (page 236, column 2, last paragraph). In addition to these cautions with respect to appropriate antigen presentation and subsequent immune responses (issue of MHC), this reference clearly indicates limited antibody responses and only some level in vitro cellular immunity with prostate specific antigen immunization. Also, this reference clearly indicates the limitations of animal models in prostate cancer modalities and that previous attempts at human prostate cancer vaccination with whole cells.

Full enablement of claims on vaccines should include teachings on the relevant immunogenic proteins and portions thereof, the level of neutralizing antibody or cellular immunity produced and the efficacy of the vaccine against subsequent inoculations of the intended pathogen, in this case a prostate tumor. Since the immune response is considered to be one of the most complex and unpredictable biological processes, without any guidance or teachings of any of the above, it is considered that it would require undue experimentation for the ordinary skilled artisan to make or to use the invention as claimed.

With respect to "immunologically effective portion thereof", the instant claims are not enabled for the breadth of "immunologically effective portion thereof". The characteristics of these antigens or portions are not clearly defined and encompasses potentially thousands of different polypeptides and peptides. The specification fails to provide sufficient guidance as to how to determine all such polypeptides and peptides. It would require undue experimentation to produce all such possible polypeptides and peptides without more explicit guidance from the disclosure.

The goal of tumor vaccination is the induction of tumor immunity to prevent tumor recurrence and to eliminate residual disease. Ezzell reviews the current thinking in cancer vaccines and states that tumor immunologists are reluctant to place bets on which cancer vaccine approach will prove effective in the long run (J. NIH Research 7: 46-49, 1995; see entire document, particularly the last paragraph; 1449). It has been well known in the art that tumor cells in vivo simply do not display their unique antigens in ways that are easily recognized by cytotoxic T lymphocytes (Ezzell; page 48, column 2, paragraph 2). Furthermore, no one is very optimistic that a single peptide or a virus carrying the gene encoding that peptide will trigger an immune response strong enough to eradicate tumors or even to prevent the later growth of micrometastases among patients whose tumors have been surgically removed or killed by radiation or chemotherapy (Ezzell; page 48, paragraph 6).

With respect to inducing prostate tumor-specific cytotoxic T lymphocytes; Peshwa et al. (The Prostate 36: 129-138, 1998) discloses that the protein sequence of PAP was evaluated using an algorithm to detect contiguous 9-amino acid peptides stretches which could potentially bind the HLA-A2 molecule; that various binding affinities were noted among the tested peptides, resulting in PAP-5 epitope as the most relevant for PAP-based therapeutic vaccines for prostate cancer (see Results); and that of the five nonapeptides shown to exhibit strong binding affinity for the HLA-A2 molecules, only PAP-5 is contained with the mature secreted PAP protein (page 136, column 1, paragraph 1).

While page 12 of the specification discloses screening for identifying peptides which may be important epitopes; applicant has not provided sufficient direction and guidance nor objective evidence in identifying or identification with "immunologically effective portions" of "over represented prostate antigens, including PSA, PSMA, PAP".

While Peshwa et al. (The Prostate, 1998) discloses that similar approaches employing dendritic cells loaded with HLA-A2 binding peptides of PSMA have been reported to have a clinical benefit (see Discussion); it appears that undue experimentation would be required of one skilled in the art to practice the claimed methods and compositions in providing effective vaccines for prostatic cancer using the teaching of the specification alone.

Insufficient direction or guidance is provided to assist one skilled in the art in the selection of all such possible "over represented antigens" and/or "immunologically active portions thereof, including PSA, PSMA and PAP" nor is there sufficient objective evidence provided that all such "antigens" and "immunologically active portions thereof" would be effective to stimulate antitumor responses .

The specification dos not provide a sufficient enabling description of the claimed invention. There is insufficient direction and guidance to enable a skilled artisans to make and use "over represented antigens" and/or "immunologically active portions thereof", as recited in the claims. A person of skill in the art would not know which "over represented antigens" or "immunologically active portions of said over represented antigens, including PSA, PAP, and PSMA" are essential or effective to stimulate antitumor responses, which "antigens"/"portions thereof" are non-essential or noneffective, and what particular lengths identify essential or effective portions. The problem of predicting polypeptide structure from mere sequence data of limited full length prostate antigens sequences and, in turn, utilizing predicted structural determinations to ascertain immunologically active portions of over represented prostate antigens and finally what changes can be tolerated with respect thereto and, in turn, which stimulate antitumor responses is complex and well outside the realm of routine experimentation

In view of the lack of predictability of the art to which the invention pertains and the lack of established clinical protocols for effective cancer vaccines and prostate cancer therapies; undue experimentation would be required to practice the claimed methods with a reasonable expectation of success, absent a specific and detailed description in applicant's specification of how to effectively practice the claimed methods and absent working examples providing evidence which is reasonably predictive that the claimed methods are effective for establishing protective antitumor responses.

7. With respect to claims drawn to nucleic acids that generate prostate antigens; the following is noted.

The incorporation of essential material in the specification by reference to a foreign application or patent, or to a publication is improper. Applicant is required to amend the disclosure to include the material incorporated by reference. The amendment must be accompanied by an affidavit or declaration executed by the applicant, or a practitioner representing the applicant, stating that the amendatory material consists of the same material incorporated by reference in the referencing application. See In re Hawkins, 486 F.2d 569, 179 USPQ 157 (CCPA 1973); In re Hawkins, 486 F.2d 579, 179 USPQ 163 (CCPA 1973); and In re Hawkins, 486 F.2d 577, 179 USPQ 167 (CCPA 1973).

An application as filed must be complete in itself in order to comply with 35 U.S.C. 112; however this does not bar incorporation by reference. Ex parte Schwarze, 151 USPQ 426 (Bd. of Appeals, 1966). an application for a patent when filed may incorporate "essential material" by reference to (1) a United States patent or (2) an allowed U.S. application, subject to the conditions set forth below. "Essential material" is defined as that which is necessary to (1) support the claims, or (2) for adequate disclosure of the invention (35 U.S.C. 112). "Essential material" may not be incorporated by reference to (1) patents or applications published by foreign countries or regional patent offices, to (2) non-patent publications, to (3) a U.S. patent or application which itself incorporates "essential material" by reference or to (4) a foreign application. See In re Fouche, 169 USPQ 429; 439 F.2d 1237 (CCPA 1971).

Nonessential subject matter may be incorporated by reference to (1) patents or application published by the United states or foreign countries or regional patent offices, (2) prior filed, commonly owned U.S. applications or (3) non-patent publications, for purposes of indicating the background of the invention or illustrating the state of the art.

The referencing application must include (1) an abstract, (2) a brief summary of the invention, (3) an identification of the referenced patent or application, (4) at least one view in the drawing in those applications admitting of a drawing, and (5) one or more claims. Particular attention should be directed to specific portions of the referenced patent or application.

As indicated above in Sections 5/6; the nucleic acids of PSA, PSMA and PAP are essential to the claimed invention. Applicant is invited to consider incorporating by reference the key nucleic acids encoding PSA, PSMA and PAP, provided there is sufficient direction and particularity of said nucleic acids in the specification as filed and providing the appropriate Hawkins Declaration. See Illustrative Antigens on pages 7-10 of the specification as filed.

8. Claim 24 is rejected under 35 U.S.C. § 112, first paragraph, as the specification does not contain a written description of the claimed invention, in that the disclosure does not reasonably convey to one skilled in the relevant art that the inventor(s) had possession of the claimed invention at the time the application was filed. The specification as originally filed does not provide support for the invention as now claimed: "wherein said is afflicted with metastatic prostate and/or where said subject has been surgically treated to excise said tumor but is at risk for recurrence".

Applicant's amendment, filed 4/28/99 (Paper No. 2), asserts that no new matter has been added; but does not provide sufficient direction for the written description for the above-mentioned "limitations".

The specification does not provide sufficient blazemarks nor direction for the instant methods encompassing the above-mentioned "limitations" as they are currently recited. The instant claims now recite limitations which were not clearly disclosed in the specification as-filed, and now change the scope of the instant disclosure as-filed. Such limitations recited in the present claims, which did not appear in the specification, as filed, introduce new concepts and violate the description requirement of the first paragraph of 35 U.S.C. 112.

Applicant is required to cancel the new matter in the response to this Office action
Alternatively, applicant is invited to provide sufficient written support for the "limitations" indicated above.
Also, see MPEP 714.02 and 2163.06

9. Claims 13 and 20-24 are rejected under 35 U.S.C. § 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

Claims 13 and 20-24 are indefinite in the recitation of "over represented antigens" because the term "over represented" is a relative term which renders the claims indefinite. The term is not defined by the claim, the specification does not provide a standard for ascertaining the requisite degree, and one of ordinary skill in the art would not be reasonably apprised of the metes and bounds of the invention.

The applicant is reminded that the amendment must point to a basis in the specification so as not to add any new matter. See MPEP 714.02 and 2163.06

10. The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CAR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103© and potential 35 U.S.C. 102(f) or (g) prior art under 35 U.S.C. 103(a).

11. Claims 13-24 are rejected under 35 U.S.C. § 103(a) as being unpatentable over Spitler (U.S. Patent No. 5,738,867 in view of Israeli et al. (U.S. Patent No. 5,538,866) and in view of art acknowledged methods of delivering antigens of interest to stimulate antitumor responses, as disclosed on pages 10-19 of the instant specification.

Spitler teaches methods of delivering antitumor vaccines with tumor associated antigens, including prostate antigens (see Summary of the Invention), as well as known methods of delivering said tumor associated antigens to stimulate antitumor responses, encompassed by the claimed invention (see entire document).

Spitler differs from the instant claimed methods by not disclosing a particular prostate antigen, nor the elected species PSMA per se.

Israeli et al. Teaches PSMA , including nucleic acids and methods of expressing said PSMA, as well as its expression on prostate tumors (see entire document, including Background of the Invention and Detailed Description of the Invention).

Pages 10-19 of the specification discloses the art known methods of delivering antigens, including tumor associated antigens, of interest to stimulate antitumor responses encompassed by the claimed methods.

Given the teachings of Israeli et al. that PSMA is useful as a marker for prostate cancer; one of ordinary skill in the art at the time the invention was made would have been motivated to substitute the prostate tumor associated antigen PSMA into the methods of stimulating antitumor responses, as known and practiced in the prior art, as taught by Spitler and acknowledged by the specification as to treat prostate cancer. It would have been obvious to the ordinary artisan to use PSMA in patients with metastatic prostate tumors and/or patients who have had the prostate tumor removed surgically to elicit antitumor responses in order to treat said cancer patients. Also, it would have been obvious to the ordinary artisan to select portions, particularly extracellular portions of PSMA to stimulate antitumor responses. From the teachings of the references and known in the prior art; it was apparent that one of ordinary skill in the art would have had a reasonable expectation of success in producing the claimed invention. Therefore, the invention as a whole was prima facie obvious to one of ordinary skill in the art at the time the invention was made, as evidenced by the references, especially in the absence of evidence to the contrary.

12. The non-statutory double patenting rejection, whether of the obvious-type or non-obvious-type, is based on a judicially created doctrine grounded in public policy (a policy reflected in the statute) so as to prevent the unjustified or improper timewise extension of the "right to exclude" granted by a patent. *In re Thorington,* 418 F.2d 528, 163 USPQ 644 (CCPA 1969); *In re Vogel,* 422 F.2d 438, 164 USPQ 619 (CCPA 1970); *In re Van Ornam,* 686 F.2d 937, 214 USPQ 761 (CCPA 1982); *In re Longi,* 759 F.2d 887, 225 USPQ 645 (Fed. Cir. 1985); and *In re Goodman,* 29 USPQ2d 2010 (Fed. Cir. 1993).

A timely filed terminal disclaimer in compliance with 37 CAR 1.321 (b) and © may be used to overcome an actual or provisional rejection based on a non-statutory double patenting ground provided the conflicting application or patent is shown to be commonly owned with this application. See 37 CAR 1.78 (d).

Effective January 1, 1994, a registered attorney or agent of record may sign a Terminal Disclaimer. A Terminal Disclaimer signed by the assignee must fully comply with 37 CAR 3.73(b).

13. Claims are rejected under the judicially created doctrine of obviousness-type double patenting as being unpatentable over claims 1-8 of U.S. Patent No. 5,925,362. Although the conflicting claims are not identical, they are not patentably distinct from each other because the patented claims are a species of instant methods.

14. No claim is allowed.

15. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Phillip Gambel whose telephone number is (703) 308-3997. The examiner can normally be reached Monday through Thursday from 7:30 am to 6:00 pm. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached on (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of such papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

PHILLIP GAMBEL

Phillip Gambel, PhD.
Primary Examiner
Technology Center 1600
October 10, 2000